

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Hermann Bujard et al.

Serial No.: N/A

Filed: June 25, 2001

(Continuation of Serial No. 09/163,269)

For: *TRANSGENIC ORGANISMS HAVING
TETRACYCLINE-REGULATED
TRANSCRIPTIONAL REGULATORY SYSTEMS (as
amended)*

Attorney Docket No.: BBI-013C2CN2

Group Art Unit:

Examiner:

Commissioner for Patents
Box Patent Application
Washington, D.C. 20231

CERTIFICATION UNDER 37 CFR 1.10

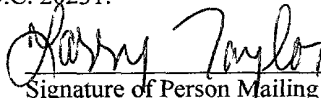
Date of Deposit: June 25, 2001

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I hereby certify that this 37 CFR 1.53(b) request and the documents referred to as attached therein are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

Larry Taylor

Name of Person Mailing Paper



Signature of Person Mailing Paper

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination of the above-identified application, please amend the application as follows:

In the Specification:

Please replace the title at page 1, line 3, and page 71, line 1 with the following new title:

**--TRANSGENIC ORGANISMS HAVING TETRACYCLINE-REGULATED
TRANSCRIPTIONAL REGULATORY SYSTEMS--.**

Please replace the paragraph beginning at page 1, line 7, under the heading "Related Applications", with the following rewritten paragraph:

--This application is a continuation of application Serial No. 09/163,269, filed September 29, 1998, pending, which is a continuation of application Serial No. 08/481,570, filed June 7, 1995, now U.S. Patent No. 5,859,310, which is a continuation-in-part of application Serial No. 08/260,452, filed June 14, 1994, now U.S. Patent No. 5,650,298, which is a continuation-in-part of application Serial No. 08/076,327, filed June 14, 1993, now abandoned, the entire contents of each of which are incorporated herein by reference.--

In the claims:

Please cancel claim 1.

Please add new claims 23-34, as follows:

--23. A transgenic organism having a transgene integrated into the genome of the organism and also having a *tet* operator-linked gene in the genome of the organism, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the organism operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which Tet repressor operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells,

said *tet* operator-linked gene confers a detectable and functional phenotype on the organism when expressed in cells of the organism,

said transgene is expressed in cells of the organism at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the organism, said fusion protein binds to the *tet* operator-linked gene and activates transcription of the *tet* operator linked gene such that the *tet* operator-linked gene is expressed at a level sufficient to confer the detectable and functional phenotype on the organism, wherein the level of expression of the *tet* operator-linked gene can be downmodulated by administering tetracycline or a tetracycline analogue to the organism.

24. A transgenic organism having a transgene integrated into the genome of the organism, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the organism operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of a *tet* operator linked gene,

the fusion protein comprising a first polypeptide which is a Tet repressor, operatively linked to a second polypeptide which directly or indirectly activates transcription in eukaryotic cells, and

said fusion protein is expressed in cells of the organism.

25. The organism of claim 23, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

26. The organism of claim 24, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

27. The organism of claim 23, wherein the transgene is integrated at a predetermined location in the genome of the organism.

28. The organism of claim 24, wherein the transgene is integrated at a predetermined location in the genome of the organism.

29. The organism of claim 27, wherein the transgene is integrated at a predetermined location such that expression of the fusion protein is controlled by 5' regulatory elements of an endogenous gene of the organism and expression of the endogenous gene is controlled by at least one *tet* operator sequence.

30. The organism of claim 28, wherein the transgene is integrated at a predetermined location such that expression of the fusion protein is controlled by 5' regulatory elements of an endogenous gene of the organism and expression of the endogenous gene is controlled by at least one *tet* operator sequence.

31. The organism of claim 23, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

32. The organism of claim 24, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.

33. The organism of claim 23, which is selected from the group consisting of: a mouse, a cow, a sheep, a pig, and a plant.

34. The organism of claim 24, which is selected from the group consisting of: a mouse, a cow, a sheep, a pig, and a plant.--

REMARKS

Claim 1 was originally filed in the application and has now been canceled. New claims 23-34 have been added. Accordingly, claims 23-34 are pending.

The title has been amended to more accurately reflect the subject matter being claimed in the application. The specification has been amended to correct the priority claim. New claims 23-34 are directed to transgenic organisms having tetracycline-regulated transcriptional regulatory systems. Support for these claims can be found

throughout the specification, and at least at, for example, page 18, lines 17-27.

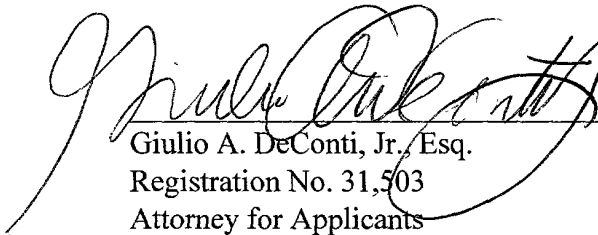
Applicants submit herewith a "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**" which indicates the specific amendments made to the title and the specification.

No new matter has been added by way of the amendments to the title, the specification, or the new claims. Applicants respectfully request that these amendments be entered.

SUMMARY

All pending claims are believed to be in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



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Dated: June 25, 2001

VERSION WITH MARKINGS TO SHOW CHANGES MADE**In the Specification:**

The title beginning at page 1, line 3 and at page 71, line 1 has been amended as follows:

~~**ANIMALS TRANSGENIC FOR A TETRACYCLINE-CONTROLLED**~~
~~**TRANSCRIPTIONAL ACTIVATOR**~~ **TRANSGENIC ORGANISMS HAVING**
TETRACYCLINE-REGULATED TRANSCRIPTIONAL REGULATORY
SYSTEMS

The paragraph beginning at page 1, line 7, under the heading "Related Applications", has been amended as follows:

This application is a continuation of application Serial No. 09/163,269, filed September 29, 1998, pending, which is a continuation of application Serial No. 08/481,570, filed June 7, 1995, now U.S. Patent No. 5,859,310, which is a continuation-in-part of application Serial No. 08/260,452, filed June 14, 1994, now U.S. Patent No. 5,650,298, which is a continuation-in-part of application Serial No. 08/076,327, filed June 14, 1993, now abandoned, the entire contents of each of which are incorporated herein by reference.